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Ivor R. Elrifi
MINTZ, LEVIN, COHN, FERRIS
GLOVSKY and POPEO, P.C.
One Financial Center
Boston, MA 02111

EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	9

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Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
10 068,426	SHAW ET AL.
Examiner	**Art Unit**
Maher M. Haddad	1644

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-53* is/are pending in the application.

4a) Of the above claim(s) *23-26 and 28-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s) _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other.

DETAILED ACTION

1. Claims 1-53 are pending.

2. Applicant's election with traverse of Group 5, claims 1-4, 6-22 and 27 drawn to a fusion polypeptide comprising SEQ ID NO: 5 filed on 11/12/02, is acknowledged.

Upon reconsideration Examiner has extended the search to cover the fusion polypeptide comprising SEQ ID NO: 1 of Group 1, claims 1-5, 10-22 and 27.

Applicant's traversal is on the grounds that Groups 1-4 and 6 fall in the same class and subclass as elected Group 5. Accordingly, no undue burden is believed presented by searching the subject matter of Groups 1-4 and 6 along with Group 5. This is not found persuasive because the specific fusion protein of GP Ibα mutants are recognized divergent subject matter. In addition, the different fusion proteins are distinct because their structures are different and are therefore capable of separate manufacture, use and sale and searches of all groups would place an undue burden upon the examiner due to the distinct and divergent subject matter of each Group.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 23-26 and 28-53 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 1-22 and 27 are under examination as they read on a fusion polypeptide comprising SEQ ID NO: 1 or SEQ ID NO: 5.

5. Claim 7 is objected to because of the following informalities: "von Willibrand" is misspelled. Appropriate correction is required.

6. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required:

Original claims 6 and 9 recite a wild-type GP Ibα1 polypeptide while the specification discloses the glycoprotein Ibα protein. If the term "Ibα" should be "Ibα1" the specification should be amended to disclose "Ibα1".

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention

8. Claims 1-4, 6-19, 21-22 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the fusion polypeptide comprising SEQ ID NO:1 or SEQ ID NO:5 for inhibiting platelet aggregation; does not reasonably provide enablement for any polypeptide comprising a first polypeptide operably linked to a second polypeptide, wherein the first polypeptide **comprises** at least any region of a glycoprotein Ibα polypeptide and the second polypeptide **comprises** at least any region of an immunoglobulin polypeptide in claim 1; wherein said first polypeptide **includes** any extracellular portion of a membrane glycoprotein Ibα polypeptide in claim 2; wherein said first polypeptide is at least 85% homolgous to SEQ ID NO:1 in claim 4, Wherein the first polypeptide is more resistant to proteolysis than any "wild-typ GP Ibα1 polypeptide" in claim 6, wherein said first polypeptide binds with hiher affinity to a von Willibrand factor polypeptide than any "wild-type glycoprotein Ibα polypeptide" binds to said von Willibrand factor polypeptide in claim 7, wherein said first polypeptide comprises at least one of the amino acid substitutions G233V or and M239V relative to the amino acid sequence of any **wild-type GPI α** polypeptide in claims 8 and 9; wherein the second polypeptide comprises any region of a heavy chain immunoglobulin in claims 10 and 15, wherein the said second polypeptide has less effector function than the effector function of a Fc region of any wild-type immunoglobuline heavy chain in claims 12 and 17 any multimeric polypeptide comprising the fusion polypeptide of claim 1 in claim 21, wherein said multimeric polypeptide is a dimer in claim 22, a pharmaceutical composition comprising the fusion polypeptide in claim 27. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not provide a sufficient enabling description of the claimed invention. The specification discloses the fusion polypeptides of SEQ ID NOs:1-6 with a disclosed activity of inhibiting an interaction between a glycoprotein Ibα ligand and a glycoprotein Ibα protein on the surface of a cell, such as a platelet (e.g., page 5 at lines 26-28). The instant claims encompass in their breadth *any* fusion polypeptide, wherein the first polypeptide comprising any region or any extracellular portion of a glycoprotein Ibα polypeptide, including those that comprise a "subsequence" (*an extracellular portion*); or wherein the first polypeptide "is at least about 85% homologous to SEQ ID NO:1"; or *any* fusion polypeptide comprises at least one of the amino acid substitutions G233V or M239V relative to the amino acid sequence of any "wilde-type GPIb α(1) polypeptide"; or wherein the second polypeptide has less effector function than the effector function of a Fc region of any "wild-type immunoglobulin heavy chain".

The specification does not provide sufficient guidance to any "wild-type glycoprotein Ibα polypeptide" or any "wild type immunoglobulin heavy chain", the skilled artisan would not know how to make and use the various wild-type glycoprotein Ibα and immunoglobulin heavy

chain recited in the claims. Further, it is noted that "wild-type" encompasses several species of naturally-occurring GP Ibα. The specification does not provide sufficient guidance that all the naturally-occurring GP Ibα polypeptides would have Gly and Met at positions 233 and 239, respectively.

There does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make and use the various fusion polypeptides recited in the instant claims. A person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences. There is insufficient guidance to direct a person of skill in the art to select particular sequences or sequence lengths as essential for inhibiting an interaction between a glycoprotein Ibα ligand and an glycoprotein Ibα protein on the surface of a platelet. Without detailed direction as to which first or second polypeptide sequences are essential to the function of the fusion polypeptide, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of fist and second polypeptide sequences encompassed by the instant claims would share the ability to inhibit platelet aggregation of the fusion polypeptide of SEQ ID NO:1 and 5, other than the fusion polypeptide of SEQ ID NO:1 and 5.

Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Finally, even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2). Thus it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

The skilled artisan would not reasonably expect a fusion polypeptide having anything less than 100% identity *over the full length of SEQ ID NO: 5* to *share the same function*. The limitation "binds to one or more of the polypeptides of a leukocyte integrin Mac-1 polypeptide, von Willebrand factor, thrombin and P-selectin" is not seen as providing a requisite functional activity for the fusion protein because, because even if the fusion polypeptide is limited in binding to the leuckocyte integrin Mac-1 polypeptide, von Willebrand factor, thrombin or P-selectin, there are still numerous functional activities encompassed besides inhibiting platelet aggregation. Thus the recitation of percent identity language, in the absence of *a testable function* and limitations regarding the *sequence length over which the percent identity is*

required; does not allow the skilled artisan to make and use the fusion polypeptides commensurate in scope with the instant claims without undue experimentation.

The terms "comprises" and "includes" in claims 1 and 2 are open-ended, they expand the first polypeptide portions of a glycoprotein Ibα to include additional non disclosed amino acids outside of the "extracellular portion" or "region". The instant claim language appears to encompass subsequences. For example, claims 1and 2 recite a fusion polypeptide comprises *at least a region* of a glycoprotein Ibα polypeptide and includes *an extracellular portion* of a membrane glycoprotein Ibα polypeptide. Such a recitation does not require that the full length of the first and the second polypeptides of fusion polypeptide sequence set forth in SEQ ID NO:1 and 5; but rather encompasses any amino acid sequence comprising either the full length of GPIbα, immunoglobulin, or *any portion*. However, the specification does not appear to have provided sufficient guidance as to which subsequences of GPIbα would share the function of inhibiting platelet aggregation. Neither does the specification appear to have provided any working examples of any functional *portions*. Thus it would require undue experimentation of the skilled artisan to determine which *portions* of the first polypeptide of SEQ ID NO:1 and 5 would have the function of the full length molecule.

There is insufficient guidance as to which portion of first polypeptide function to inhibit platelet aggregation and whether the resulting polypeptide would maintain the same function as binding to one or more of the polypeptides of leuckocyte integrin Mac-1 polypeptide, von Willebrand factor, thrombin or P-selectin. Ngo *et al* teach that the amino acid positions within the polypeptide protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). Given the lack of sufficient guidance and working examples, predicting what changes can be made to the amino acid of the first polypeptide sequence of SEQ ID NO: 1 and 5 that after modification will retain the same structure of a glycoprotein Ibα is unpredictable.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the changes which can be made in the instantly recited fusion polypeptide sequences and still maintains the functional properties of the fusion polypeptide of SEQ ID NO:1 and 5 is unpredictable, as is the identity of which subsequences would encode a functional polypeptide; thus the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

11. Claims 1-4, 6-19, 21-22 and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of the fusion polypeptide comprising SEQ ID NO:1 or SEQ ID NO:5 for inhibiting platelet aggregation.

Applicant is not in possession of any polypeptide comprising a first polypeptide operably linked to a second polypeptide, wherein the first polypeptide comprises at least any region of a glycoprotein Ibα polypeptide and the second polypeptide comprises at least any region of an immunoglobulin polypeptide in claim 1; wherein said first polypeptide includes any extracellular portion of a membrane glycoprotein Ibα polypeptide in claim 2; wherein said first polypeptide is at least 85% homolgous to SEQ ID NO:1 in claim 4, Wherein the first polypeptide is more resistant to proteolysis than any "wild-typ GP Ibα1 polypeptide" in claim 6, wherein said first polypeptide binds with hiher affinity to a von Willibrand factor polypeptide than any "wild-type glycoprotein Ibα polypeptide" binds to said von Willibrand factor polypeptide in claim 7, wherein said first polypeptide comprises at least one of the amino acid substitutions G233V or and M239V relative to the amino acid sequence of any wild-type GPI α polypeptide in claims 8 and 9; wherein the second polypeptide comprises any region of a heavy chain immunoglobulin in claims 10 and 15, wherein the said second polypeptide has less effector function than the effector function of a Fc region of any wild-type immunoglobuline heavy chain in claims 12 and 17 any multimeric polypeptide comprising the fusion polypeptide of claim 1 in claim 21, wherein said multimeric polypeptide is a dimer in claim 22, a pharmaceutical composition comprising the fusion polypeptide in claim 27.

Applicant has disclosed the fusion polypeptide of SEQ ID NO: 1-6; therefore, the skilled artisan cannot envision all the contemplated fusion polypeptide sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does

not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1-5, 10-22 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over in Lopez JA et al (Proc Natl Acad Sci U S A. 84:5615-5619, 1987) view of U.S. Patent No. 6,277,975.

Lopez *et al* teach a 626 amino acid glycoprotein Ibα (including the signal sequence of 16 amino acids) that is a platelet receptor for von Willebrand factor comprising a region of a glycoprotein Ibα polypeptide which includes an extracellular portion. The vWf and thrombin binding domain of GP Ibα, which contains seven tandem repeats of the conserved leucine-rich sequence resides within the amino terminus of the molecules (see page 5618, figure 5 and abstract in particular). The N-terminal region (aa 1-318 of SEQ ID NO:1) is 100% identical to the first polypeptide of the fusion polypeptide (see sequence alignment in particular).

The claimed invention differs from the reference teachings only by the recitation of a fusion protein wherein the second polypeptide comprises a region of a heavy chain immunoglobulin polypeptide in claims 10 and 15, wherein the said second polypeptide comprises an Fc region of

an immunoglobulin heavy chain in claims 11 and 16, wherein said second polypeptide has less effector function that the effector function of a Fc region of a wild-type immunoglobulin heavy chain in claims 12 and 17, wherein said second polypeptide binds with low or no affinity to a Fc receptor in claims 13 and 18, wherein said second polypeptide binds with low or no affinity to complement protein C1q in claims 14 and 19; a multimeric polypeptide comprising the fusion protein in claim 21, wherein the multimeric polypeptide is a dimmer in claim 22.

The '975 patent teaches the P-selectin ligand fusion protein comprises a 313 amino acid sequence (see reference SEQ ID NO: 36 in particular) comprising Fc portion of a human of IgGγ1 (column 11, lines 40-41 in particular) with 100% homology with amino acids 318-544 of claimed SEQ ID NO: 1 (see sequence alignment in particular). The '975 patent further teaches that Fc portion of native or mutated immunoglobulin sequences for conferring desirable qualities such as longer half-life or reduced immunogenicity (see column 10 lines 37-40 in particular). Finally, the '975 patent teaches pharmaceutical compositions comprising the P-selectin ligand proteins (column 4, lines 48-50 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to link the glycoprotein Ibα region taught by Lopez *et al* with Fc portion of a human IgGγ1 taught by the '975 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because Fc portion of native or mutated immunoglobulin sequences conferring desirable qualities such as longer half-life or reduced immunogenicity as taught by the '972 patent and the vWf-binding domain of GP Ibα resides within the amino terminus of the molecule taught by Lopez et al.

The claimed functional limitation of claims 12-14 and 17-19 would be expected properties of the referenced Fc region of a human of IgGγ1 because the claimed and reference Fc region are 100% identical. Products of identical chemical composition can not have mutually exclusive properties. A chemical composition and its properties are inseparable.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

14. Claims 1-4, 6-19, 21-22 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over in Miura *et al* (J Biol Chem. 275:7539-7546) view of U.S. Patent No. 6,277,975.

Miura *et al* teach a GPIbα-calmodulin fusion protein (aa residues His^{1}-Val^{289}) of GPIbα (GPIbα-CaM), Ibαwt, Ibα233V, Ibα239V and Ibα233V239V (as in instant claim 9 and claimed SEQ ID NO:5) (see page 7540 under Expression and purification of GPIbα proteins in particular). Miura et al further teach GPIbα mutaions G233V and M239V with increase in affinity of VWF A1 for

GPIbα(M239V)-CaM and GPIbα(M233V)-CaM (see abstract in particular). Miura *et al* teach that platelet adhesion requires the binding of VWF to the platelet membrane glycoprotein Ib-IX (extracellular portion) and the binding site for VWF is in the N-terminal 293 residues of GPIbα. Finally, Miura et al teach the GPIba-CaM (or variant) in Tris-HCl buffer. (see page 7539, right column, 1st paragraph in particular).

The claimed invention differs from the reference teachings only by the recitation of that the fusion protein, wherein said first polypeptide is more resistant to proteolysis than a wild-type GP Ibα1 polypeptide in claim 6; the fusion protein wherein the second polypeptide comprises a region of a heavy chain immunoglobulin polypeptide in claims 10 and 15, wherein the said second polypeptide comprises an Fc region of an immunoglobulin heavy chain in claims 11 and 16, wherein said second polypeptide has less effector function that the effector function of a Fc region of a wild-type immunoglobulin heavy chain in claims 12 and 17, wherein said second polypeptide binds with low or no affinity to a Fc receptor in claims 13 and 18, wherein said second polypeptide binds with low or no affinity to complement protein C1q in claims 14 and 19, a multimeric polypeptide comprising the fusion protein in claim 21, wherein the multimeric polypeptide is a dimmer in claim 22.

The '975 patent teaches the P-selectin ligand fusion protein comprises a 313 amino acid sequence (see reference SEQ ID NO: 36 in particular) comprising Fc portion of a human of IgGγ1 (column 11, lines 40-41 in particular) with 100% homology with amino acids 318-544 of claimed SEQ ID NO: 1 (see sequence alignment in particular). The '975 patent further teaches that Fc portion of native or mutated immunoglobulin sequences for conferring desirable qualities such as longer half-life or reduced immunogenicity (see column 10 lines 37-40 in particular). Finally, the '975 patent teaches pharmaceutical compositions comprising the P-selectin ligand proteins (column 4, lines 48-50 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the Calmodulin peptide taught by Miura *et al* with Fc portion of a human IgGγ1 taught by the '975 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because Fc portion of native or mutated immunoglobulin sequences conferring desirable qualities such as longer half-life or reduced immunogenicity as taught by the '972 patent.

Claim 6 is included because the claimed and reference first polypeptide are the same in the absence of evidence to the contrary and therefore, the claimed limitation of more resistant to proteolysis than wild-type GPIbα1 polypeptide is considered inherent properties.

The claimed functional limitation of claims 12-14, 17-19 and 21-22 would be expected properties of the referenced Fc region of a human of IgGγ1 because the claimed and reference Fc region are 100% identical. Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. Claims 1, 5 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miura *et al* (J Biol Chem. 275:7539-7546) view of U.S. Patent No. 6,277,975 as applied to claim 1-4, 6-19, 21-22 and 27 above, and further in view of U.S Patent No. 5,340,727.

The teachings of Miura *et al* reference and the '975 patent, has been discussed, supra.

The claimed invention differs from the reference teachings only by the insertion of a signal peptide MPLLLLLLLLPSPLHP which result in SEQ ID NO:1 and 5 in claims 5 and 20.

The '727 patent teaches that the predicted GPIba sequence consists of a 16 amino acid signal peptide, MET^{-16} through PRO^{-1}, followed by a 610 amino acid mature peptide region, HIS^{1} through LEU^{610} amino acid (see column 2 lines 39-49 in particular). The '727 patent further teaches that the signal peptide when attached to the amino terminal end of the residue 1-610 or 1-302 GPIbα polypeptide, the signal peptide causes the polypeptide to be recognized by cellular structures as a polypeptide of the kind to be processed for ultimate secretion from the cell, with concomitant cleavage of the signal polypeptide from the mature GPIbα polypeptide (column 14 lines 52-64 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to insert the signal peptide taught by the '727 patent in the amino terminal end of the 1-289 GPIbα polypeptide taught by Miura *et al* and then link the resultant GPIbα polypeptide with the Fc portion of a human IgGγ1 taught by the '975 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the signal peptide causes the polypeptide to be recognized by cellular structures as a polypeptide of the kind to be processed for ultimate secretion from the cell, with concomitant cleavage of the signal polypeptide from the mature GPIbα polypeptide as taught by the '727 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
January 27, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600